CASE: MA0095 NP

DEC 14 2005

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Burton Rodney

Type or print name

Signature

Date

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

**ART UNIT: 1623** 

MANOJ NERURKAR ET AL.

EXAMINER: MAIER, LEIGH C

**APPLICATION NO: 10/642,366** 

FILED: 08/14/2003

FOR: ARIPIPRAZOLE COMPLEX FORMULATION AND METHOD

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

# <u>DECLARATION OF PRIOR INVENTION OF MANOJ NERURKAR AND VIJAY NARINGREKAR TO OVERCOME CITED U.S. PATENT PUBLISHED APPLICATION U.S. 2002/0193438 A1 (37 C.F.R. §1.131)</u>

To the Commissioner for Patents and Trademarks:

- 1. This Declaration is to establish reduction to practice of the invention in this application at a date prior to April 25, 2001, that is the priority date claimed in U.S. 2002/0193438 A1.
  - 2. Manoj Nerurkar and Vijay Naringrekar declare as follows.
- 3. That they are employed by Bristol-Myers Squibb Company, the assignee of the subject application as evidenced by an assignment signed by each and recorded at the U.S. Patent and Trademark Office on September 17, 2003, Reel 103985, Frame 0962 (ATTACHMENT I).

4. That they are the inventors, together with Mark Dominick, of the invention claimed in U.S. patent application Serial No. 10/642,366 filed August 14, 2003.

- 5. That the invention defined in the claims as filed was conceived and reduced to practice in the United States prior to April 25, 2001.
- 6. That prior to April 25, 2001 Manoj Nerurkar and Vijay Naringrekar conceived of the concept of solubilizing aripiprazole by complexing it with a β-cyclodextrin and Mark Dominick together with Manoj Nerurkar and Vijay Naringrekar conceived of an injectable aripiprazole formulation which produces minimal irritation at the injection site.
- 7. That prior to April 25, 2001, Manoj Nerurkar carried out experiments to increased solubility of aripiprazole by forming complexes of aripiprazole with various β-cyclodextrins, such experiments being recorded in Bristol-Myers Squibb Notebook No. 42671 cover page (ATTACHMENT A) and pages 122, 132, 133, 134, 135 and 136, copies of which pages are attached hereto and identified as ATTACHMENTS B, C, D, E, F and G, respectively.
- 8. On Notebook page 122 (ATTACHMENT B), entitled "Project No. 030D8, Experiment No. 44, Solubility Screening Studies with BMS-337039 (Aripiprazole)", Manoj Nerurkar recorded experiments which he carried out prior to April 25, 2001, wherein he prepared a mixture of aripiprazole in 10% hydroxypropyl β-cyclodextrin in water (HPBCD) and in 10% sulfobutyl ether β-cyclodextrin (SBECD) in water, whereby it is seen that solubility of aripiprazole was improved from 0.0001 mg/mL in water to 0.02 mg/mL in HPBCD and 0.12 mg/mL in SBECD.

Page 122 was signed by Manoj Nerurkar and witnessed by Sunita Borsadia prior to April 25, 2001, the effective date as a reference of U.S. 2002/0193438 A1.

9. On Notebook pages 132, 133 and 134 (ATTACHMENTS C, D and E, respectively), entitled "Project No. 030D81, Experiment No. 49, Combination of pH adjustment and SBECD complexation", Manoj Nerurkar recorded experiments which he carried out prior to April 25, 2001,

wherein the objective was "to determine if SBECD forms a complex with aripiprazole either in ionized or salt form of a drug". Pages 132, 133 and 134 describe preparation of solutions of complexes of aripiprazole and SBECD (Captisol®) in HCl (Batch A) or in lactic acid (Batch B) having a pH ranging from 4.12 to 5.2 (Batch A in HCl).

Notebook pages 132, 133 and 134 were signed by Manoj Nerurkar and witnessed by Sunita Borsadia prior to April 25, 2001, the effective date as a reference of U.S. 2002/1093438 A1.

10. On Notebook pages 135 and 136 (ATTACHMENTS F and G, respectively), entitled "Project 030D8, Experiment No. 50, Effect of Increasing Conc. of Cyclodextrins (SBECD) on Equilibrium Solubilities of BMS-337039-01 [Aripiprazole] at Various pHs" Manoj Nerurkar recorded experiments which he carried out prior to April 25, 2001. As seen on pages 135 and 136, solutions of aripiprazole in 5, 10, 15 and 20% SBECD and a solution of aripiprazole in 20% HPBCD were prepared, each of whose pH was adjusted with HCl. As seen in the second table on page 136, solubility of the aripiprazole in the SBECD and HPBCD increased markedly with decreasing pH.

As seen on page 122, solubility of aripiprazole in water is 0.0001 mg/mL. As seen on page 136, solubility of aripiprazole in 5% SBECD at pH ranging from 6.4 to 4.8 has a solubility ranging from 0.65 to 7.29 mg/mL; aripiprazole in 10% SBECD at pH ranging from 6.4 to 4.8 has a solubility ranging from 1.31 to 14.51 mg/mL; aripiprazole in 15% SBECD at pH ranging from 6.4 to 4.8 has a solubility ranging from 2.11 to 18.19 mg/mL and aripiprazole in 20% SBECD at pH ranging from 6.4 to 4.8 has a solubility ranging from 2.7 to 24.96 mg/mL.

It is therefore concluded that the increase in solubility of the aripiprazole is due to its complexation with the  $\beta$ -cyclodextrin which clearly establishes reduction to practice of the invention as claimed.

11. Manoj Nerurkar signed each of the pages 135 and 136 but inadvertently failed to date his signature. However, Sunita Borsadia witnessed both pages by signing and dating both pages prior to April 25, 2001. Accordingly, it can only be concluded that Manoj Nerurkar signed the notebook pages 135 and 136 prior to April 25, 2001.

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12. The actual dates of Experiments 44, 49 and 50 were carried out and the dates of signing by Manoj Nerurkar and witnessing by Sunita Borsadia, were all prior to April 25, 2001, but have been obliterated.

- 13. The above clearly establishes conception and reduction to practice of the invention covered by the relevant claims of the subject patent application (vis-à-vis U.S. published patent application 2002/0193438) prior to April 25, 2001.
  - 14. This Declaration is submitted prior to Final Rejection.
- 15. The undersigned declares further that all statements made herein of their own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of application Serial No. 10/642,366 or any patent issued thereon.

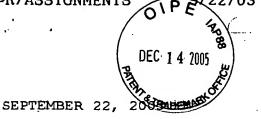
Date: Dec 7, 2005

Date: Dec. 7, 200)

MANOJ NERURKAR

Y-NARINGREKAR

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BRISTOL-MYERS SQUIBB COMPANY STEPHEN B. DAVIS P.O. BOX 4000 PRINCETON, NJ 08543-4000 UNITED STATES DEPARTMENT OF COMMERCE Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231



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UNITED STATES PATENT AND TRADEMARK OFFICE NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 09/17/2003

REEL/FRAME: 013985/0962

NUMBER OF PAGES: 6

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

NERURKAR, MANOJ

DOC DATE: 09/03/2003

ASSIGNOR:

NARINGREKAR, VIJAY

DOC DATE: 09/03/2003

ASSIGNOR:

DOMINICK, MARK

SERIAL NUMBER: 10642366

DOC DATE: 09/15/2003

08/14/03

**ASSIGNEE:** 

BRISTOL-MYERS SQUIBB COMPANY LAWRENCEVILLE-PRINCETON ROAD PRINCETON, NEW JERSEY 08543-4000

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FILING DATE:

ISSUE DATE:

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PATENT NUMBER:

013985/0962 PAGE 2

TONYA LEE, EXAMINER ASSIGNMENT DIVISION OFFICE OF PUBLIC RECORDS

PK/ASSIGNMENTS 9/22/03 4:39 1 SEP.17.2003 2:26PM P 589 257 4526	PAGE 4/4 RIGHTFAX NO.397 P.Z P.Z
FORM PTO-1595 RECOR TO	Patent and Trademark Office
OMB No. 0551-0011 (exp. 494) DEC: 1 4 2005 PATENTS	ONLY
To the Hangmala Direction the US Parent and Trademark Of	fice: Please record the attached original documents or copy thereof.
	2. Name and address of receiving party(ies)
Name of conveying party(les);     Manoj Nerurkar, Vijay Naringrekar, Mark	Name: Bristol-Myers Squibb Company
Dominick	
Dollinger	Internal Address:
Additional name(s) of conveying party(les) attached?   Yes  No	
3. Nature of conveyance:	
☑ Assignment ☐ Merger	Street Address: Lawrenceville-Princeton Road
Security Agreement Change of Name	
Other	City: Princeton State: NJ ZIP: 08543-4000
Execution Date: September 3, 2003, September 15.	Additional name(s) & address(es) attached? 🔲 Yes 🗵 No
2003	
4. Application number(s) or patent number(s): If this document is being filed together with a new application	the execution date of the application is:
A. Patent Application No.(s)	B. Patent No.(s)
10/642,386	
Additional muniphas	ached? ☐ Yes ⊠ No
Name and address of party to whom correspondence concerning document should be mailed:	Total number of applications and patents involved:
Name: Stephen B. Davis	7. Total fee (37 CFR 3.41) \$40
Internal Address: Bristol-Myers Squibb Company	☐ Enclosed
Patent Department	Authorized to be charged to deposit account and any other additional fees required.
Street Address: P.O. Box 4000	8. Deposit account number:
City: Princeton State: NJ ZIP: 08543-4000	19-3880 (in the name of Bristol-Mivers Squibb Company) (Attach duplicate copy of this page if paying by deposit account)
DO NOT L	ISE THIS SPACE
9. Statement and signature. To the best of my knowledge and belief, the foregoing.	Information is true and correct and any attached copy is a true
copy of the original document.	) . N <u>.</u> 0
Burton Rodney Name of Person Signing	September 17, 2003  Date
T N- 00 076	mailing on reverse side
Total number of pages including con	ver sheet, attachments, and document: 6

#### **ASSIGNMENT**

We,

Manoj Nerurkar residing at 83 Regal Drive

Monmouth Junction, New Jersey 08852

United States of America

Vijay Naringrekar residing at 538 Burlington Street

Paramus, New Jersey 07652

United States of America

Mark Dominick residing at 10540 Wilmington Drive Evansville, Indiana 47725

United States of America,

pursuant to contractual obligations heretofore assumed by us and/or for good and valuable consideration, the receipt and adequacy of which is hereby acknowledged, do hereby sell and assign to **Bristol-Myers Squibb Company**, a Delaware corporation, having a place of business at Lawrenceville-Princeton Road, Princeton, NJ 08543-4000, its successors, assigns and legal representatives, all our right, title and interest, which includes the right to and full benefit of such priorities as may now or hereafter be granted to us by local laws or by treaty, including any international convention for the protection of industrial property, in and for all countries of the world, including the United States and its territories and possessions, in and to the invention entitled:

#### ARIPIPRAZOLE COMPLEX FORMULATION AND METHOD

invented by us and described in the non-provisional United States patent application

Application No. 10/642,366, filed August 14, 2003,

including said non-provisional United States patent application and any application claiming priority from said non-provisional application, filed in any country, and any patents which may be issued and/or granted thereon, and all divisions, continuations, reissues, reexamination certificates and extensions thereof in all countries, the said interest being the entire ownership of said invention and all of said applications, patents (including reissue patents), extensions and reexamination certificates to be held and enjoyed by the said Bristol-Myers Squibb Company and its successors and assigns to the full end of the terms to which said patents (including reissue patents), extensions and reexamination certificates may be granted and/or issued, as fully and entirely as the same would have been held and enjoyed by us if this sale, assignment and transfer had not been made;

And we hereby agree to communicate to said assignee or its representatives any facts known to us respecting said invention, to testify in any legal proceedings, to sign and/or execute any further documents and/or instruments which may be necessary, lawful and proper in and/or for the filing and/or prosecution of all applications, including divisional, continuation and reissue applications, extensions and reexamination certificates and/or the granting and/or issuance thereof and/or to otherwise secure title to said invention and all of said applications, patents (including reissue patents, extensions and reexamination certificates in said assignee, and in general to do everything possible to aid said assignee, its successors and assigns to obtain and enforce proper protection for said invention in all countries.

Manoj Nefurkar	Signed this 3 day of September 2003 by	Mans veres car
		Manoj Nerurkar

STATE OF New Jersey ) ss. COUNTY OF Middleser )

On the 3rd day of September, 2003, before me came Manoj Nerurkar, to me known to be the person of that name mentioned in, and who executed the foregoing Assignment and acknowledged that he/she executed it.

[SEAL]

LAURA H. DERBIN
NOTARY PUBLIC, STATE OF NEW JERSEY
ID # 2278973
Commission Expires Sept. 7, 2006

Signed this 3 day of Set	stember, 2003 by	Viay Naringrekar	 <del></del>
STATE OF New Jussey COUNTY OF Middlesex	) ) ss. )		

On the 3rd day of September, 2003, before me came Vijay Naringrekar, to me known to be the person of that name mentioned in, and who executed the foregoing Assignment and acknowledged that he/she executed it.

[SEAL]

LAURA H. DERBIN
NOTARY PUBLIC, STATE OF NEW JERSEY
ID # 2278973
Commission Expires Sept. 7, 2006

Signed this 5th day of Sophe.	<u>mber</u> , 2003 by	Mark Dominick	il
STATE OF	)		
COUNTY OF	) ss. )		
On the 15th day of Septem the person of that name mer acknowledged that he/she execution	ntioned in, and who		
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[SEAL]		Linda Jo , Notary Publi	Henrman c

# BRISTOLIMYERS SQUIBB

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M.Nesuskas

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### BRISTOL-MYERS SQUIBB PHARMACEUTICAL RESEARCH INSTITUTE

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CASE: MA0095 NP



#### CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Burton Rodney

Type or print name

Signature

Dec. 12,2005

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

**ART UNIT: 1623** 

MANOJ NERURKAR ET AL.

EXAMINER: MAIER, LEIGH C

**APPLICATION NO: 10/642,366** 

FILED: 08/14/2003

FOR: ARIPIPRAZOLE COMPLEX FORMULATION AND METHOD

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

#### **DECLARATION OF SUNITA BORSADIA**

To the Commissioner for Patents and Trademarks:

#### SUNITA BORSADIA DECLARES AS FOLLOWS:

- 1. She has a Master's degree and is a scientist specializing in pharmaceutics and pharmaceutical formulations (Pharma R&D).
- 2. She has been employed in the above capacity at Bristol-Myers Squibb Company for 8 years.
- 3. She is familiar with the laboratory experiments carried out by Manoj Nerurkar concerning preparation of aripiprazole complexes with  $\beta$ -cyclodextrins.

CASE: MA0095 NP

4. She signed as a witness laboratory notebook entries made by Manoj Nerurkar in Notebook No. 42671, pages 122, 132, 133, 134, 135 and 136 (Attachment A, cover page, and Attachments B, C, D, E, F and G, respectively).

5. All of the above notebook pages were signed by Manoj Nerurkar prior to April 25, 2001.

6. All of the above notebook pages were witnessed by her prior to April 25, 2001.

7. She is not an inventor of the subject matter claimed in U.S. Application Serial No. 10/642,366.

8. The undersigned declares further that all statements made herein of her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of application Serial No. 10/642,366 or any patent issued thereon.

Date: 11125/05

SUNITA BORSADIA

# BRISTOL-MYERS SQUIBB

PHARMACEUTICALRESEARCHINSTITUTE

### BRISTOL – MYERS SQUIBB PHARMACEUTICAL RESEARCH INSTITUTE

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_ Triacetin							3.5	• • •	Nerui	kam\ar	ipi\41980	)22 ,	
1% Egg Lecithin +1% Bile Salts (So. Cholate+deoxycholate) in water							0.05	•	Nerui	kam\ar	ipi\41980	)23	
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